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Loss of Total and Visceral Adipose Tissue Mass Predicts Decreases in Oxidative Stress After Weight Loss Surgery

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Abstract

It is not known whether there are mechanisms linking adipose tissue mass and increased oxidative stress in obesity. This study investigated associations between decreasing general and abdominal fat depots and oxidative stress during weight loss. Subjects were severely obese women who were measured serially at baseline and at 1, 6 ($n = 30$), and 24 months ($n = 18$) after bariatric surgery. Total fat mass (FAT) and volumes of visceral (VAT) and subcutaneous abdominal adipose tissue (SAT) were related to plasma concentrations of derivatives of reactive oxidative metabolites (dROMS), a measure of lipid peroxides and oxidative stress. After intervention, BMI significantly decreased, from $47.7 \pm 0.8 \text{ kg/m}^2$ to $43.3 \pm 0.8 \text{ kg/m}^2$ (1 month), $35.2 \pm 0.8 \text{ kg/m}^2$ (6 months), and $30.2 \pm 1.2 \text{ kg/m}^2$ (24 months). Plasma dROMS also significantly decreased over time. At baseline, VAT ($r = 0.46$), FAT ($r = 0.42$), and BMI ($r = 0.37$) correlated with 6-month decreases in dROMS. Similarly, at 1 month, VAT ($r = 0.43$) and FAT ($r = 0.41$) correlated with 6-month decreases in dROMS. Multiple regression analysis showed that relationships between VAT and dROMS were significant after adjusting for FAT mass. Increased plasma dROMS at baseline were correlated with decreased concentrations of high-density lipoprotein (HDL) at 1 and 6 months after surgery ($r = -0.38$ and -0.42). This study found longitudinal associations between general, and more specifically intra-abdominal adiposity, and systemic lipid peroxides, suggesting that adipose tissue mass contributes to oxidative stress.

INTRODUCTION

The world is experiencing an epidemic of obesity that affects (in 2005) >500 million adults, with the highest rates in the United States (30%), Europe (20%), and the Middle East (20–25%) (1). As obesity increases the risk of developing metabolic diseases, including diabetes, cardiovascular disease, hypertension, cancer, dyspnea, and osteoarthritis (2), the prevalence of these diseases is expected to rise, and this is expected to overburden public health systems. Given the size of the problem, it will be important to identify pathophysiological factors potentially related to obesity to define effective prevention and treatment strategies.

DISCLOSURE

The authors declared no conflict of interest.

Oxidative stress is commonly identified in many obesity-related diseases and may be the mechanism underlying the progression/initiation of these diseases. Oxidative stress can be assessed *in vivo* by measurement of the products of free radical damage to lipids, proteins, and DNA in biological fluids (3). Multiple studies have shown the relationship between biomarkers of oxidative stress and obesity. Obese individuals show higher concentrations of plasma isoprostanes (4), plasma malondialdehyde (5), skeletal muscle 4-hydroxynonenal (6), and plasma protein carbonyls (7,8). Severity of obesity is also inversely correlated with specific antioxidant enzyme activities, including that of CuZn superoxide dismutase and glutathione peroxidase (9).

Limited data suggest that regimens promoting weight loss result in decreased indices of oxidative stress in obese individuals. Individuals maintained on a weight-loss diet for 4 weeks showed a decrease in weight correlated with a decrease in thiobarbituric reactive acid substances, protein carbonyls, and oxidation of linoleic acids (13-HODE and 9-HODE) in blood (7). Although these results suggest a relationship between body fat and oxidative stress, changes may also be due, in part, to the low-fat/carbohydrate and low-calorie diet itself, as diet has been shown to modulate systemic oxidative stress (10,11). These variables make the evaluation of the contribution of body fat to systemic oxidative stress difficult.

In this study, systemic oxidative stress was determined in severely obese individuals after bariatric surgery–induced weight loss. Patients were measured at baseline (before weight loss) and serially for up to 24 months after surgery. During the study, we determined markers of oxidative stress, using the derivatives of reactive oxidative metabolites (dROMS) test, which measures plasma peroxides, and plasma nitrotyrosine, which measures oxidized amino acids. Data show decreases in systemic oxidative stress with weight loss and a longitudinal relationship between adiposity and oxidative stress.

METHODS AND PROCEDURES

Patients

The study subjects were 30 severely obese female patients who had weight-loss treatment at the Emory Bariatrics Center either via laparoscopic roux-en-y gastric bypass surgery ($n = 28$), or via adjustable banding ($n = 2$) (12). This was a longitudinal study in which each patient served as her own control. Subjects were evaluated at baseline (before surgery) and at 1, 6, and 24 months after surgery. Subjects were eligible for surgery after evaluation (clinical, psychological, and nutritional) when they were recruited for the study. Exclusion criteria were (i) male gender, (ii) age <18 years or >65 years, (iii) BMI <35 kg/m², and (iv) current smoking history. All medication, including that used to treat metabolic syndrome, was monitored throughout the study. For a subset of consecutively enrolled subjects, diet history, using 3-day food records, was collected at each study visit and analyzed using Food Processor SQL (ESHA Research, Salem, OR).

Measurements of glucose tolerance, anthropometry, adipose tissue distribution, oxidative stress, and plasma inflammatory biomarkers were obtained at baseline (before treatment) and at 1, 6, and 24 months after surgery. During the week before the baseline, 6-month, and 24-month postsurgery time points, subjects were weight stable (± 1 kg) (13). These steady-state conditions were not feasible at the time of the 1-month weight-loss studies, when patients were showing ~3 kg/week weight loss, but measures were obtained at this time to capture potentially informative variables. Medications were withheld from patients on the morning of glucose tolerance testing.

Glucose tolerance testing

Insulin action was assessed using the frequently sampled intravenous glucose tolerance test. Patients were admitted into the Emory General Clinical Research Center on the night before testing and fasted over-night (12 h). An intravenous catheter was inserted into an antecubital vein for blood sampling. Baseline samples were obtained at -15 and -5 min. Glucose (0.3 g/kg body weight, as dextrose 50 g/dl) was then administered within 2 min, and subsequent samples were obtained at 2, 4, 6, 8, 10, 14, 19, 22, 24, 27, 30, 40, 50, 70, 90, 120, 150, 180, 210, and 240 min relative to the start of glucose infusion. At 20 min, subjects received an intravenous bolus of human insulin (0.02 U/kg body weight). Minimal modeling analysis of glucose and insulin levels (14) was used to quantify insulin sensitivity, insulin secretion, and the disposition index (MinMod Millennium, Los Angeles, CA). Fasting concentrations of glucose and insulin were used to calculate the homeostatic model assessment measure of insulin resistance, $\text{HOMA-IR} = \text{insulin } (\mu\text{U/ml}) \times \text{glucose (mmol/l)} / 22.5$ (15).

Anthropometry, body composition, and fat distribution

Body fat composition was measured by air plethysmography (BOD-POD; Life Measurement Instruments, Concord, CA). Abdominal fat distribution was measured by computed tomography, using a GE High Speed Advantage scanner (General Electric Medical Systems, Milwaukee, WI) as described elsewhere (16). Volumes of visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT) were determined from scans taken in the L1–L5 vertebral region (140 kV, 240–340 mA·s, 10 mm slice thickness). Adipose tissue within an attenuation range of -190 to -30 Hounsfield units was highlighted and computed using software (General Electric Medical Systems). In our scanner we are able to analyze patients with body weight up to 182 kg (400 lb). Sagittal abdominal diameter was obtained at the L4–L5 intervertebral space using an abdominal caliper (17). Body height was measured without shoes. Body weight was measured with subjects in light clothing, in the fasting state, and immediately after voiding in the morning. Waist circumference was taken using a tape measure at 2.54 cm above the iliac crest, and hip circumference was determined as the maximum value over the buttocks.

Metabolic measures

Serum insulin and glucose concentrations were quantified at the Emory University Hospital Laboratory using the Beckman Coulter DX1 and Beckman Coulter Alex 20 automated systems, respectively (Beckman Coulter, Brea, CA). The limit of the assay for insulin was 1 $\mu\text{U/ml}$ and that for glucose was 0.17 mmol/l. Plasma leptin was measured using a commercial human enzyme-linked immunosorbent assay kit (Diagnostic Systems Laboratory, Webster, TX). The inter- and intraassay variability were 4.4 and 4.0%, respectively. Plasma resistin, adiponectin, IL-6 (high sensitivity), and TNF- α (high sensitivity) were measured using commercial human enzyme-linked immunosorbent assay kits (R&D Systems, Minneapolis, MN). Serum high-sensitivity C-reactive protein was measured using the SYNCHRON LX20 high-sensitivity immunoassay (Beckman Coulter, Fullerton, CA). The sensitivity of the assay is 0.07 mg/dl. Free fatty acids were measured by ARUP Laboratories (Salt Lake City, UT). Oxidative stress was measured in plasma using the dROMS assay, which measures serum hydroperoxide levels (dROMS Test; Diacron, Grosseto, Italy). This parameter has been used to measure oxidants in blood, and its usefulness as a biomarker has been demonstrated in several studies (18–21). Plasma concentrations of nitrotyrosine and tyrosine were measured by mass spectrometry following procedures reported previously (22). In brief, each sample was delipidated, desalted, and hydrolyzed for 24 h under an argon atmosphere. Amino-acid hydrolysates were resuspended and washed using mini solid-phase C18 extraction columns and then analyzed using liquid chromatography with tandem mass spectrometry (SCIEX API 3000; Applied Biosystems, Foster City, CA). Nitrotyrosine and tyrosine levels were determined by stable isotope-labeled standards, 3-nitro($^{13}\text{C}_9$ $^{15}\text{N}_1$)tyrosine and tyrosine ($^{13}\text{C}_9$ $^{15}\text{N}_1$), respectively.

Statistical analysis

The statistical software STATISTICA (StatSoft, Tulsa, OK) was used for analysis. The differences between baseline and 1-, 6-, and 24-month postsurgery measures were analyzed using paired Student's *t*-tests. The relationships between changes in various metabolic and anthropometrical parameters were examined as linear correlations using Pearson's correlation coefficient. Data that were not normally distributed were analyzed using Spearman's rank order correlations. For most relationships, significant correlations were observed whether or not subjects who underwent adjustable banding were excluded. The significance level was set at $P < 0.05$. Results are expressed as mean \pm s.e.m.

The Emory University Institutional Review Board approved the study, and all patients gave informed consent before they were enrolled.

RESULTS

Baseline patient characteristics

Thirty subjects completed the full longitudinal analysis up to 6 months after surgery, and 18 of these were evaluated again at 24 months. At baseline, their average age was 36.1 ± 1.6 years (range 24–55 years), and 20% of the women were postmenopausal. Nine women were self-described as non-Hispanic blacks, 17 were non-Hispanic whites, one was Native American, and three were Hispanic. The mean BMI was 47.7 ± 0.8 kg/m² (range 39.4–55.3 kg/m²). All women had abdominal obesity (waist circumference >88 cm), and 22 subjects (73% of patients) had two other criteria of Adult Treatment Panel III–defined metabolic syndrome (low high-density lipoprotein (HDL), high triglycerides, hypertension, and/or glucose intolerance) (23). Six patients (20% of the population), had type 2 diabetes as defined elsewhere (24) and were taking medication to improve insulin action.

Changes in adiposity and anthropometry after weight-loss surgery

After bariatric surgery, patients experienced weight loss as a result of reduction in energy intake from $1,695 \pm 99$ to 821 ± 172 kcal/day at 1 month and $1,128 \pm 105$ kcal/day at 6 months (both $P < 0.05$, obtained from 3-day food records; $n = 8$ –13). At 24 months after surgery, caloric intake was 1,433 kcal/day. No significant changes were observed in dietary macronutrient content (carbohydrate, fat, and protein) as a percentage of energy intake during the 24-month period after surgery (data not shown). Changes in anthropometry during the 24-month period are reported in Table 1. The two surgical interventions achieved similar weight loss; therefore the data were pooled for analysis. Compared with baseline, significant decreases were observed in both fat mass (FAT) and lean body mass at 1, 6, and 24 months after surgery, but more fat than lean mass was lost at all time points ($P < 0.000$). In the acute 1-month period after surgery, subjects lost VAT but not SAT in the abdominal area; they experienced decreases in both depots at 6 and 24 months. Subjects lost a higher percentage of VAT than of SAT at 1, 6, and 24 months after surgery ($P < 0.000$ for 1 and 6 months; $P < 0.05$ at 24 months). Also, sagittal abdominal diameter was significantly decreased from baseline as early as 1 month after surgery, and waist circumference was not significantly decreased until 6 months after surgery.

Changes in cardiometabolic risk factors after weight-loss surgery

The number of subjects with Adult Treatment Panel III–defined metabolic syndrome decreased from 76% at baseline to 41%, 21%, and 24% at 1, 6, and 24 months, respectively ($P < 0.05$, compared with baseline; Table 2). Compared with baseline, HDL concentrations worsened at 1 month and increased by 24 months after surgery, but they remained abnormally low in 53% of subjects. In this series of subjects, we reported earlier that glucose tolerance improved at 6 months after surgery as a result of selective changes in hepatic insulin resistance (homeostatic

model assessment measure of insulin resistance), β -cell function (acute insulin response to glucose and disposition index), and peripheral insulin sensitivity, and diabetes was resolved in all but one patient by 6 months after surgery (25). In this article we report similar changes in these parameters in these patients during the 24-month period after surgery and relationships to changes in oxidative stress.

Changes in oxidative stress after weight-loss surgery

Oxidative stress, measured by the dROMS lipid peroxides assay, progressively decreased during weight loss, from 0.047 ± 0.003 absorbance units at baseline to 0.039 ± 0.003 at 1 month, 0.027 ± 0.002 at 6 months, and 0.020 ± 0.002 at 24 months ($P < 0.05$; Figure 1). As a measure of oxidatively damaged proteins, plasma concentrations of nitrotyrosine (N-Tyr) were measured and normalized to plasma tyrosine (Tyr) levels. N-Tyr measured in a subset of four individuals was increased from baseline (1.5 ± 0.4 nmol N-Tyr/mol Tyr) at 1 month after surgery (2.8 ± 0.6 nmol N-Tyr/mol Tyr) and then decreased compared with baseline at 6 months (1.0 ± 0.3 nmol N-Tyr/mol Tyr) and 24 months (0.7 ± 0.3 nmol N-Tyr/mol Tyr) ($P < 0.05$ in all cases).

Relationships between oxidative stress and anthropometry

The time since surgery had a significant effect on systemic dROMS concentrations over the 24-month period ($P < 0.05$) (Figure 1). To determine whether decreased measures of oxidative stress were associated with decreasing adiposity, linear cross-sectional and longitudinal correlation analyses were performed between plasma dROMS and various measures of adiposity. Larger preoperative measures of VAT, waist circumference, FAT, BMI, and body weight predicted larger decreases in dROMS during the initial 6-month period of postsurgical weight loss (Figure 2). In contrast, no significant relationship was observed between preoperative SAT and dROMS over time (data not shown). In addition, 1-month-postsurgery measures of VAT, FAT, BMI, and body weight predicted 6-month reduction in dROMS (Figure 3). The correlations between change in dROMS and VAT volumes were stronger than the correlations with FAT mass. Also, multiple regression analysis (Table 3) showed that the relationship between the change in dROMS levels and preoperative or 1-month measures of VAT mass remained significant when adjusting for FAT mass. In contrast, the relationships between FAT and dROMS were no longer significant after adjusting for VAT. This suggests that visceral adiposity makes a more specific contribution to systemic dROMS concentrations than general adiposity. In addition, a correlation approaching significance was observed between baseline VAT volumes and the change in dROMS over 24 months ($r = 0.41$, $P = 0.09$, $n = 18$). No relationship was found between FAT mass and changes in dROMS over the same period ($r = 0.13$, $P = 0.6$). These results, taken together, strongly suggest that changes in plasma dROMS concentrations, which represent systemic lipid peroxides, may be regulated by adiposity, with visceral adiposity playing the largest role. No cross-sectional relationships were observed between adiposity variables and dROMS at any specific time point. In addition, no cross-sectional or longitudinal relationships were observed between lean mass, dietary carbohydrate, fat, or protein intake and plasma dROMS concentration during any of the measurement periods.

Relationships between oxidative stress and cardiometabolic risk

We examined relationships between oxidative stress and measures of cardiometabolic risk and glucose metabolism at baseline and during weight loss. Plasma HDL concentrations at 1 and 6 months were negatively predicted by the baseline plasma dROMS concentrations ($r = -0.38$ and -0.42 , $P = 0.05$ and 0.02 , respectively) (Figure 4). HDL concentrations were not associated with any measures of adiposity, and FAT as a covariate in multivariate analysis did not confound the relationship between dROMS and HDL (data not shown). Although dROMS was

found to be associated with measures of adiposity shown to be risk factors for glucose intolerance, no correlations were found between plasma dROMS and insulin resistance or β -cell function.

DISCUSSION

The major findings of this study are that markers of oxidative stress indicative of damaged lipids (dROMS) and proteins (nitrotyrosine) are decreased in severely obese women followed during weight loss for 24 months. Increased baseline measures of adiposity, including total fat mass and VAT volume, predicted larger postoperative falls in lipid peroxides, suggesting that adipose tissue contributes to systemic oxidative stress. Furthermore, plasma lipid peroxide concentrations negatively predicted HDL levels. These data point to a close relationship between central adiposity, oxidative stress, and cardiometabolic risk.

Insulin resistance and other features of metabolic syndrome are commonly found in obesity, but the mechanisms linking these phenomena are not fully understood. To explore causal mechanisms, we tested longitudinal relationships between general and central adiposity, diabetogenic adipokines, and metabolic syndrome in studies of severely obese women undergoing weight loss via bariatric surgery. We previously demonstrated in this series of subjects that changes in systemic inflammation owing to decreased C-reactive protein and increased adiponectin predicted improved peripheral and hepatic insulin resistance measured *in vivo* using the frequently sampled intravenous glucose tolerance test (25,26). As oxidative stress has been shown to be increased in obesity and inflammatory states (27), we determined whether decrease in fat mass over a period of 24 months after bariatric surgery would affect measures of oxidative stress and whether decreases in oxidative stress would correlate to improvements in cardiometabolic risk.

Data from this study suggest that adipose tissue contributes to systemic concentrations of oxidatively modified lipids. Plasma lipid peroxides measured by dROMS specifically and persistently decreased with decreasing adiposity over the period of weight loss of 24 months. The decrease in lipid peroxides over 6 months of weight loss was predicted by baseline as well as 1-month postoperative measures of adiposity. More specifically, visceral adiposity appeared to contribute independently to changes in dROMS when compared to general adiposity. Changes in dROMS over 6 months of weight loss were more predictable by adiposity measures than those changes measured over 1 and 24 months of weight loss. Also interesting is that no cross-sectional relationships were observed between adiposity variables and dROMS at any time point. Taken together, these data suggest that the effects of adipose tissue on dROMS are more apparent during dynamic states of weight loss, such as from baseline to 6 months, than during states of minimal weight loss or during weight stability. Future studies should determine the kinetics and regulation of the formation of lipid peroxides from adipose tissue.

An increase in markers of oxidative damage in obesity (5,28–30) and reduction after weight loss intervention such as bariatric surgery (8,31), caloric restriction for 4 weeks (7) and 12 months (32), exercise for 6 months (33,34), and orlistat pharmacotherapy for 6 months (35) has been shown. Consistent with our study findings, some of these intervention studies (33, 35) demonstrated longitudinal relationships between BMI and lipid peroxides. As we obtained more precise measures of fat and lean mass, as well as dietary analysis, our study demonstrates, for the first time, specific associations between adiposity and lipid peroxides—a measure of oxidative damage. Plasma nitrotyrosine, another measure of oxidative stress, also decreased in a small subset of study subjects over the 24-month weight-loss period. The findings in our study demonstrate that associations between obesity and oxidative stress are also found in states of extreme obesity and during weight loss.

In support of the observational data in this and the aforementioned human studies, accumulating evidence supports the concept that adipose tissue contributes to systemic lipid peroxides and that this contribution is exaggerated with increasing adiposity. Recent studies have demonstrated that reactive oxygen species production increased (29), and an oxidized redox state (36) was found in adipose tissue of obese compared with lean rodents. Also, in obese states, increasing amounts of macrophages and lymphocytes reside in adipose tissue and, in combination with adipocytes, may release free radicals (37–40). Macrophage concentrations decrease in adipose tissue in patients undergoing weight loss (41,42). Taken together, this evidence suggests that factors associated with adipose tissue may generate oxidized lipid by-products and that the quantity and/or activity of these factors diminishes during weight loss.

In terms of adipose tissue distribution, this study's findings and those of recent cross-sectional studies propose that visceral fat is more strongly associated with oxidative stress than abdominal subcutaneous fat or general adiposity (43,44). The approach used in this study was more informative than that of other studies, as we took direct measures of abdominal VAT and SAT volumes and of total fat mass during weight loss. We report that relative to total fat mass, intra-abdominal adiposity as determined by VAT volumes appears to be a stronger determinant of oxidative stress. Whether visceral and subcutaneous adipose depots vary in oxidation status has not been determined in humans. However, limited evidence suggests that antioxidant defenses, including catalase and glutathione peroxidase, were reduced in epididymal (intra-abdominal) fat pads in obese Zucker rats compared with those in inguinal (subcutaneous) fat pads (36).

Diabetes (45) and cardiovascular disease (46), as well as cardiometabolic risk factors, dyslipidemia (47), insulin resistance (48), and hypertension (49), have been characterized by increased oxidative stress. In this study, we found that preoperative plasma dROMS negatively predicted postoperative systemic HDL concentrations. HDL is known to have antioxidant properties owing to associated paraoxonase enzyme activity (50). This enzyme inactivates lipid peroxides and reduces the accumulation of oxidized lipids in LDL, and its activity is inversely correlated with severity of cardiovascular disease (51). Our observations suggest that high systemic peroxides at baseline may have adverse and long-term effects on concentrations of HDL. This finding may explain why HDL concentrations were low preoperatively and did not normalize for many subjects until after 6 months postsurgery. Potential mechanisms mediating the effects of lipid peroxides on concentrations and antioxidant capacity of HDL remain to be explored.

Although longitudinal correlations were found in this study linking fat mass and central adiposity to oxidative stress, and oxidative stress to HDL, which are established biomarkers of cardiometabolic risk, these findings are observational. The heterogeneity of study subjects with respect to race and glucose tolerance can be regarded as both a strength and weakness of the study. The relationships reported appeared to be uniform, as findings were similar whether or not subjects with diabetes were included. Although diet composition was not found to predict changes in dROMS, we acknowledge that these measures were obtained from self-reported measures of food take, which are known to be less precise. Further studies with larger sample sizes, including men and also subjects undergoing lifestyle (diet and exercise) and pharmacological interventions, may reveal whether longitudinal associations between oxidative stress and obesity are to be found in other populations of patients during weight loss. Also, it is important to note that although various assays are used to measure oxidative damage, this study measured primarily lipid peroxides. Thus, the effects of fat mass on other oxidatively damaged molecules remain to be determined.

In summary, we here demonstrate, for the first time in a longitudinal clinical study, that VAT volume and, to a lesser extent, total adipose tissue mass are specific determinants of plasma

concentrations of lipid peroxides—an indicator of systemic oxidative stress. Thus, oxidative stress decreased as adipose tissue decreased during weight loss in the acute and long-term periods. We showed that baseline concentrations of plasma lipid peroxides were related to decreases during weight loss in concentrations of HDL, which functions as an antioxidant. Taken together, our data suggest that adipose tissue volumes determine indices of systemic oxidative stress, which, in turn, may be involved in the etiology linking obesity to cardiometabolic disease.

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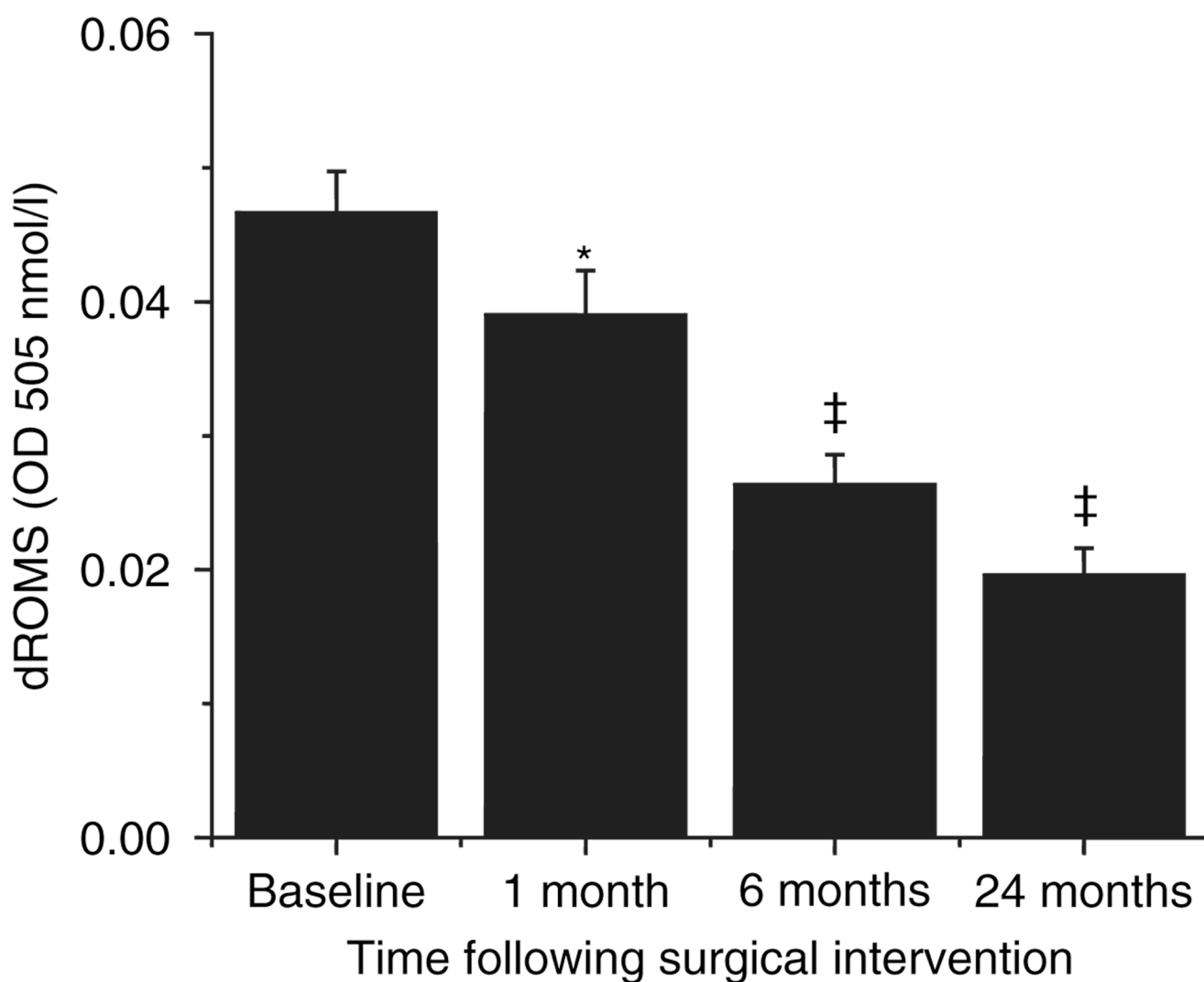


Figure 1.

Changes in systemic concentrations of lipid peroxides in severely obese subjects during 24 months after bariatric surgery. Plasma was collected and stored at baseline and 1, 6, and 24 months ($n = 30, 28, 30$, and 18 , respectively) and assessed for lipid peroxides using the derivatives of reactive oxidative metabolites (dROMS) assay. * $P < 0.05$, ‡ $P < 0.0001$ compared to baseline using paired Student's t -tests.

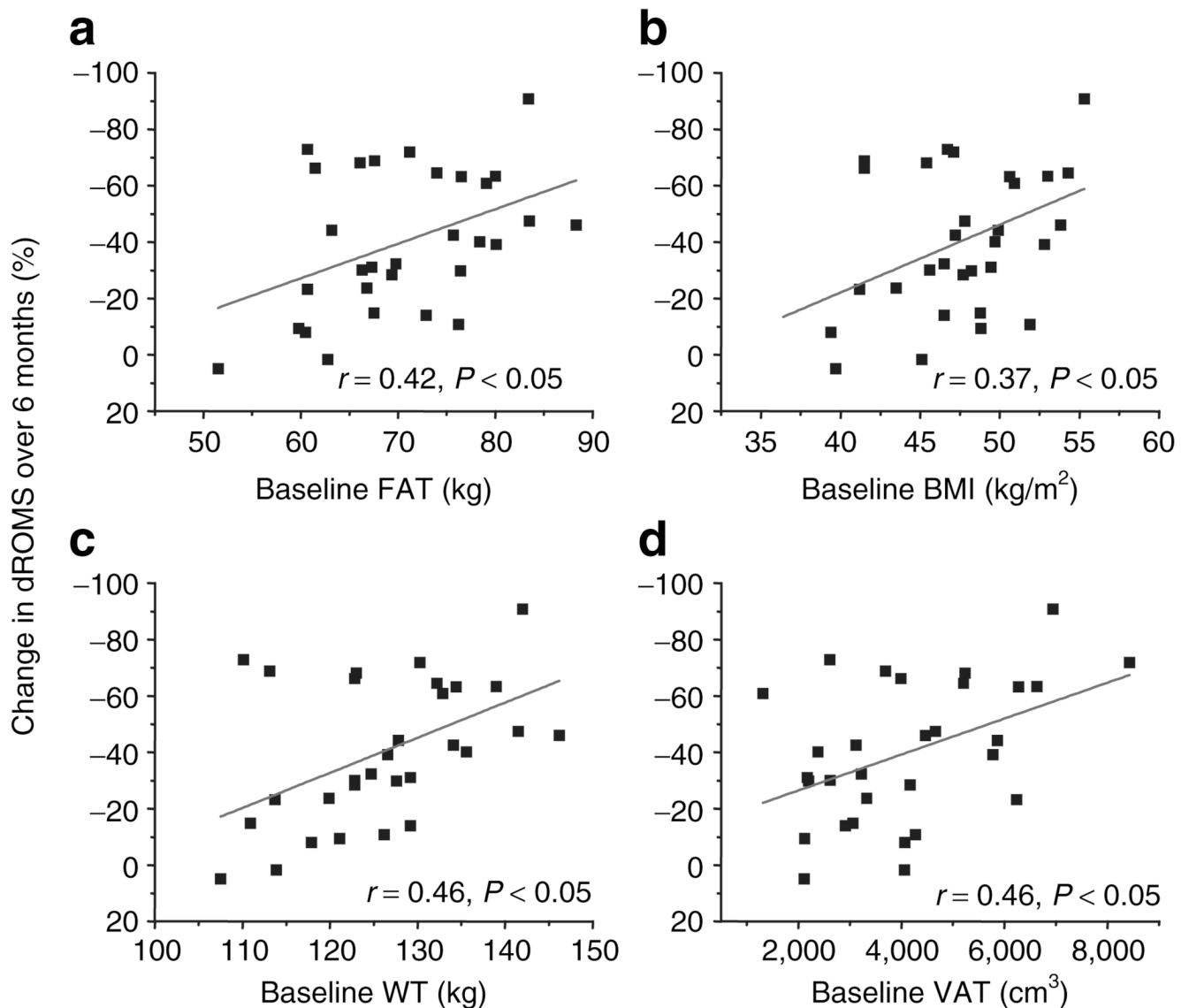


Figure 2.

Correlations between baseline measures of adiposity and changes in dROMS over 6 months after surgery. Pearson's correlation coefficients (r) between percentage changes in plasma derivatives of reactive oxidative metabolites (dROMS) over 6 months and (a) preoperative body fat mass (FAT), (b) BMI, (c) body weight (WT), and (d) abdominal visceral adipose tissue volumes (VAT) were determined ($n = 30$). As indicated in the figure, all correlation coefficients were significant.

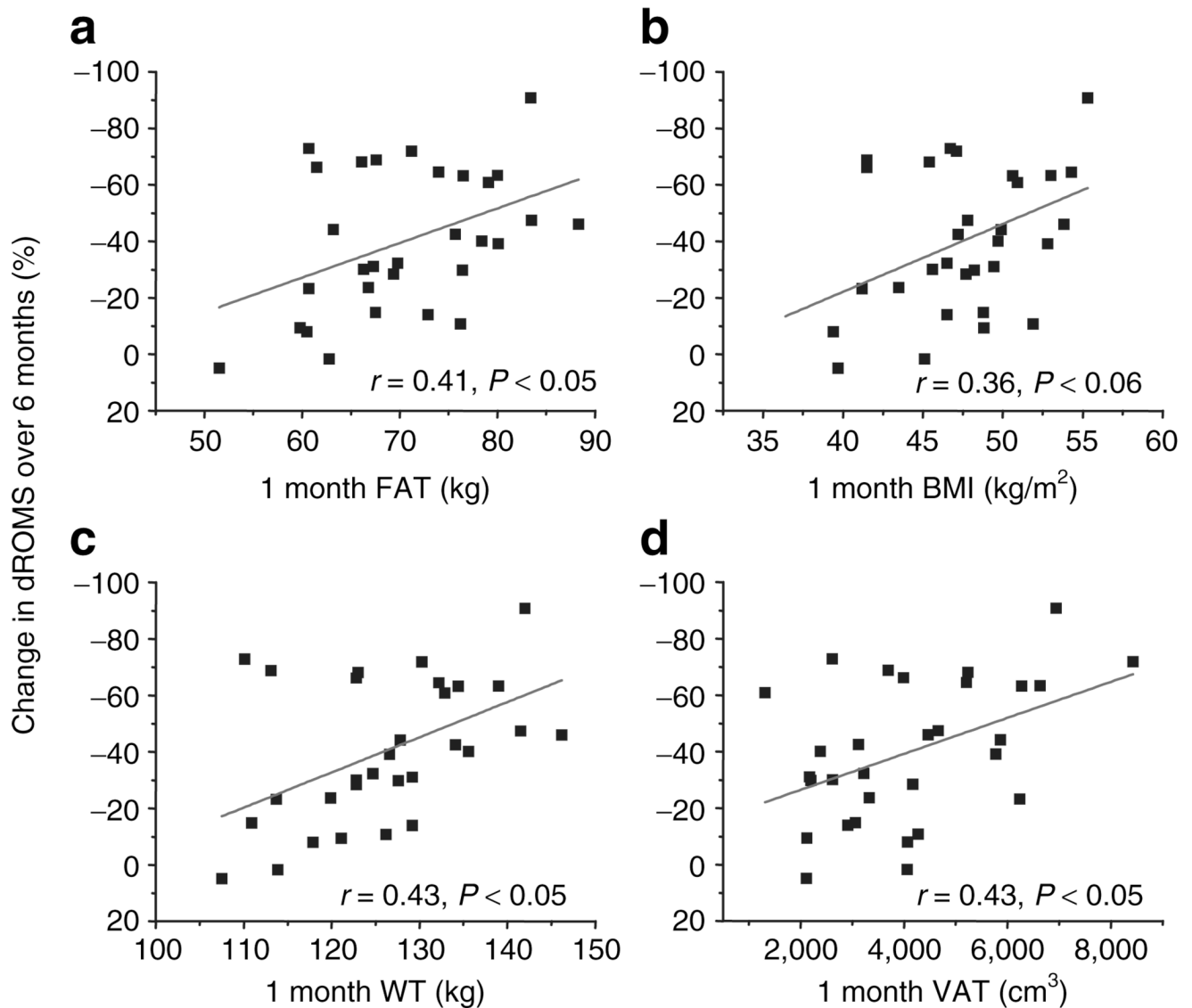


Figure 3.

Pearson's correlation coefficients (r) between percentage changes over 6 months in systemic dROMS and (a) body fat mass (FAT), (b) BMI, (c) body weight (WT), and (d) abdominal visceral adipose tissue volumes (VAT) at 1 month after surgery were determined ($n = 29$). As indicated in the figure, correlation coefficients between dROMS and VAT, FAT, and WT were significant.

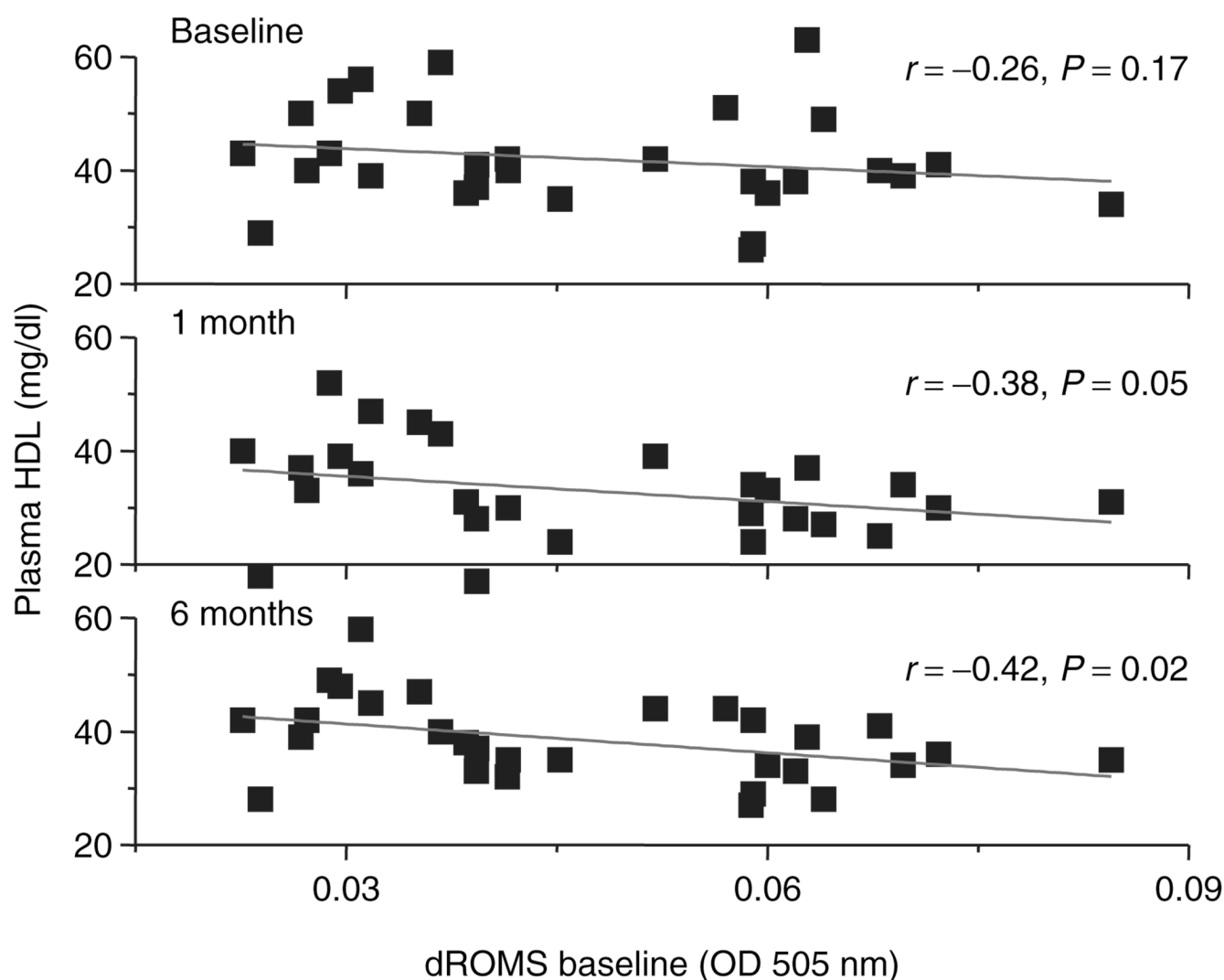


Figure 4.

Correlations between systemic concentrations of lipid peroxides and high-density lipoproteins (HDLs). Spearman's correlation coefficients (r) were determined for preoperative plasma dROMS vs. plasma HDL concentrations at baseline and 1 and 6 months after surgery ($n = 29$, 27, and 29, respectively). As indicated in figure, correlations between baseline dROMS and HDL concentrations at 1 and 6 months after surgery were significant ($P < 0.05$).

Table 1
Changes in anthropometry in 30 severely obese patients from baseline to 24 months after bariatric surgery

	Baseline	1 month	Δ 1 month	6 months	Δ 6 months	2 years	Δ 2 years
Weight (kg)	126 ± 1.8 (107.5–146.2)	114.6 ± 1.7 (95.7–133.7)	–11.7 [‡]	92.9 ± 2.1 (73.0–127.7)	–33.1 [‡]	79.2 ± 3.2 (50.4–114.7)	–45.9 [‡]
Fat mass (kg)	70.6 ± 1.6 (51.5–88.3)	62.3 ± 1.4 (44.5–76.3)	–8.7 [‡]	42.0 ± 1.7 (30.0–72.7)	–28.6 [‡]	31.5 ± 2.5 (14.3–58.7)	–38.9 [‡]
Lean mass (kg)	55.0 ± 0.9 (43.4–64.6)	51.8 ± 0.9 (41.1–60.7)	–3.2 [‡]	50.6 ± 0.8 (38.2–56.4)	–4.4 [‡]	47.5 ± 1.2 (36.1–53.9)	–7.1 [‡]
BMI (kg/m ²)	47.7 ± 0.8 (39.7–55.3)	43.3 ± 0.8 (35.4–52.2)	–4.4 [‡]	35.2 ± 0.8 (29.2–48.0)	–12.5 [‡]	30.2 ± 1.2 (21.6–44.8)	–17.7 [‡]
VAT (cm ³)	4,100 ± 320 (1,310–8,430)	3,660 ± 310 (1,410–7,490)	–520 [‡]	2,380 ± 250 (490–5,850)	–1,730 [‡]	1,420 ± 330 (270–6,390)	–2,480 [‡]
SAT (cm ³)	12,790 ± 350 (7,362–17,660)	12,340 ± 380 (7,800–17,810)	–480	8,570 ± 360 (3,780–12,730)	–4,230 [‡]	6,410 ± 720 (1,850–14,610)	–6,790 [‡]
WC (cm)	134.8 ± 2.4 (112.5–165.0)	129.2 ± 2.4 (106.5–163.0)	–5.0 [‡]	112.4 ± 2.6 (89.0–130.0)	–22.6 [‡]	94.4 ± 3.1 (78.6–127.0)	–40.8 [‡]
SAD (cm)	30.3 ± 0.4 (26.0–34.0)	28.0 ± 0.5 (24.0–33.3)	–2.2 [‡]	23.9 ± 0.5 (19.5–29.2)	–6.4 [‡]	21.4 ± 0.7 (15.2–29.5)	–8.9 [‡]

Data are means ± s.e.m. (range). At baseline and 1, 6, and 24 months after surgery, $n = 30$, 28, 30, and 18, respectively.

Δ change in measures from baseline; SAD, sagittal abdominal diameter; SAT, subcutaneous adipose tissue; VAT, visceral adipose tissue; WC, waist circumference.

* $P < 0.05$

[‡] $P < 0.01$

^{‡‡} $P < 0.001$.

Table 2
Changes in anthropometry in 30 severely obese patients from baseline to 24 months after bariatric surgery

	Baseline	1 month	Δ 1 month	6 months	Δ 6 months	2 y	Δ 2 y
Glucose (mmol/l)	5.55 ± 2.29 (3.67–10.67)	4.44 ± 0.17 (3.39–7.72)	–1.16 [†]	4.29 ± 0.10 (3.39–6.61)	–1.26 [*]	4.06 ± 0.10 (3.50–5.00)	1.58 [*]
Insulin (μU/ml)	13.32 ± 1.14 (2.00–32.04)	7.62 ± 0.78 (2.0–16.46)	–6.09 [‡]	5.05 ± 0.68 (1.00–18.4)	–8.27 [‡]	3.35 ± 0.33 (1.00–5.50)	–10.40 [‡]
HOMA (mmol/l·μU/ml)	3.33 ± 0.35 (0.58–8.06)	1.57 ± 0.21 (0.32–4.98)	–1.87 [‡]	1.02 ± 0.18 (0.17–5.41)	–2.31 [‡]	0.61 ± 0.06 (0.17–1.18)	–2.63 [‡]
Si (10 ⁴ mU/l)·min ^{–1}	1.88 ± 0.22 (0.20–6.39)	1.94 ± 0.24 (0.06–4.47)	0.30	3.20 ± 0.30 (1.09–8.84)	1.32 [†]	5.16 ± 0.55 (2.11–9.89)	3.41 [‡]
AIRg (μU/ml·min)	479 ± 87 (–18–1,610)	594 ± 1.39 (16–3,200)	63.7	374 ± 49 (26–1,230)	–105	347 ± 43 (115–768)	–107
Disposition index (min ^{–1})	680 ± 106 (–34–1,610)	782 ± 113 (15–2,105)	–82	977 ± 103 (202–2,199)	297	1,670 ± 228 (475–3,915)	902 [†]
hsCRP (mg/dl)	1.29 ± 0.21 (0.37–4.50)	1.27 ± 0.23 (0.25–4.82)	–0.04	0.56 ± 0.10 (0.02–1.90)	–0.73 [†]	0.13 ± 0.04 (0.02–0.47)	–0.96 [†]
Systolic blood pressure (mm Hg)	135 ± 4 (104–193)	127 ± 3 (102–166)	–8 [*]	122 ± 3 (93–158)	–13 [†]	124 ± 4 (88–166)	–4 [†]
FFA (mmol/l)	0.70 ± 0.04 (0.21–1.11)	1.03 ± 0.05 (0.67–1.68)	0.33 [‡]	0.73 ± 0.04 (0.38–1.33)	0.02	0.52 ± 0.04 (0.26–0.99)	–0.22
HDL (mg/dl)	42 ± 2 (29–63)	33 ± 2 (18–52)	–7 [†]	38 ± 1 (27–58)	–4	51 ± 3 (36–81)	9 [*]
Triglycerides (mg/dl)	124 ± 11 (43–300)	100 ± 6 (52–203)	–27 [*]	95 ± 9 (38–230)	–27 [*]	76 ± 7 (30–135)	–24 [*]
Metabolic syndrome (number of patients (%))	22 (76)	11 (41)		6 (21)		4 (24)	
Low HDL (number of patients (%))	20 (69)	24 (83)		25 (86)		4 (53)	

Data are means ± s.e. (range). Metabolic syndrome and low-HDL criteria are as defined by the American Heart Association (52). At baseline and 1, 6, and 24 months after surgery, $n = 29$, 24, 29, and 17, respectively.

^{*} $P < 0.05$

[†] $p < 0.01$
[#] $p < 0.001$.

Δ change in measures from baseline; AIR_g, acute insulin response to glucose; FFA, free fatty acids; HDL, high-density lipoprotein; HOMA, homeostatic model assessment; hsCRP, high-sensitivity C-reactive protein; Si, insulin sensitivity.

Table 3

Relationships between change in dRoMs over 6 months and measures of adiposity using multiple regression analysis

		Adjusted for FAT	Adjusted for VAT
VAT baseline	0.46	0.38	
VAT 1 month	0.43	0.36	
FAT baseline	0.42		n.s
FAT 1 month	0.41		n.s

Relationships, reported as Pearson's correlation coefficients, between changes in derivatives of reactive oxidative metabolites (dROMS) over 6 months of weight loss and visceral adipose tissue volumes (VAT) or fat mass (FAT) at baseline and 1 month after surgery were determined using linear regression followed by multiple regression analysis by adjusting for FAT or VAT, respectively. Only significant relationships are shown.

$P < 0.05$, n.s. = not significant; $n = 30$ at baseline and $n = 29$ at 1 month.